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Food and Drug Administration
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STATEMENT OF

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FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

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INTRODUCTION

Good morning, Chairman Rush and Members of the Subcommittee. I am Dr. Norris Alderson, Associate Commissioner for Science at the U.S. Food and Drug Administration (FDA or the Agency), part of the Department of Health and Human Services (HHS). FDA appreciates the opportunity to discuss our ongoing work regarding the safety of bisphenol A (BPA).

In light of recent reports and statements from the National Toxicology Program (NTP) at the National Institutes of Health, Health Canada, and interested public health advocates, FDA believes it is important that consumers have accurate and up-to-date information about BPA. We have established an Internet page at *http://www.fda.gov/oc/opacom/hottopics/bpa.html*, where consumers can find such information.

On April 17, 2008, FDA Commissioner Andrew von Eschenbach formed an Agency-wide BPA Task Force, which I chair, to conduct a review, encompassing all FDA-regulated product lines, of the concerns raised about BPA. The task force is undertaking a broad review of current research and information on BPA. In addition to looking at the food and beverage containers that have been the focus of recent concerns as well as our regulatory efforts over the years, the task force is conducting an inventory of all products regulated by FDA's food and medical products centers to better understand other potential routes of exposure. We are already looking at the specific concerns raised by NTP in its recent Draft Brief and the draft risk assessment released by Health Canada last month.

At this time, FDA is not recommending that consumers discontinue using food contact materials that contain BPA. Although our review of the NTP reports is continuing, a large body of available evidence indicates that food contact materials containing BPA currently on the market are safe, and that exposure levels to BPA from these materials, including exposure to infants and children, are below those that may cause health effects. We also acknowledge that BPA research is an extremely active area, and we want to assure you that if FDA's review of data leads us to a determination that uses of BPA are not safe, the Agency will take action to protect the public health.

REGULATION OF COMPONENTS OF FOOD CONTACT MATERIALS CONTAINING BPA

BPA is used in the manufacture of two types of polymers used in food contact articles, specifically, polycarbonate polymers and epoxy-based enamels and coatings. These food contact substances have been regulated for many years pursuant to regulations published in Title 21 of the *Code of Federal Regulations* (CFR). Polycarbonate (PC) polymers, which are found in products such as water and infant bottles, are regulated in 21 CFR §177.1580. Epoxy-based enamels and coatings, which are widely used as inner linings for food cans, are regulated in 21 CFR §175.300 (b) (3) (viii), 21 CFR §177.1440 and 21 CFR §177.2280. Because no polymeric reactions go entirely to completion, small residual amounts of BPA can remain in polymers and may migrate into food during use of the product. For this reason, FDA's safety assessments include a consideration of likely consumer exposure, which I will describe shortly. From these assessments, the Agency has determined that dietary exposure to

BPA from these uses is in the very low parts per billion range, which is well below the levels that would cause adverse health effects. Further, it is important to emphasize that as new data and reviews of BPA have become available, FDA's review of the safety of BPA has been an ongoing process.

EVALUATION OF BPA SAFETY

Although FDA has been actively surveying data on BPA for many years, the Agency began a formal reassessment of the chemical in early 2007. This reassessment initially focused on possible "low-dose" effects for BPA but, in the fall of 2007, we added an evaluation of the endpoints identified by an expert panel of the NTP's Center for the Evaluation of Risks to Human Reproduction (CERHR) after the CERHR meeting in August 2007.

In evaluating the safety of food contact articles or their constituents, such as BPA, FDA's safety assessment relies on evaluating probable consumer exposure as a result of the proposed use and other authorized uses, and ensuring that the probable consumer exposures are supported by the available toxicological information. With regard to consumer exposure, FDA found that the small amounts of BPA that migrated into food from the use of PC-based polymers and BPA-based epoxy coatings result in a cumulative daily intake for adults of 11 micrograms per person per day (µg/person/day).

This estimate is based on: 1) the migration levels of BPA into food, or into food-simulating solvents, under the most severe conditions of use (i.e., time and temperature), and 2)

information on the types of food contacted, the fraction of the diet that would come into contact with that type of food contact material, and whether the finished food contact article would be intended for single or repeated use. FDA's evaluation also considered that the use of can enamels in infant formula packaging and the use of PC baby bottles results in an estimated daily intake of 7 µg/infant/day. These estimates relied on data generated by FDA laboratories or the regulated industry, or available in the open literature, on BPA levels in canned food and in food contacting PC articles.

In conducting this evaluation, FDA was aware that higher migration levels had been reported in some studies available in the literature. Many of those studies were conducted under very unrealistic conditions, such as the use of aggressive solvents or extremely high temperatures that are not reflective of how the products were intended to be used by consumers. Those studies were deemed to not be representative of actual use conditions. In our evaluation of consumer exposure, we used exposure assumptions that while based on realistic scenarios, tended to over-estimate consumer exposure.

FDA's reassessment of possible "low-dose" effects of BPA concluded that the current level of exposure to adults and infants is safe as defined in 21 CFR §170.3(i). This conclusion was based on our review of the most relevant data available at that time, including our analyses, completed in July 2007, of two pivotal multi-generational oral studies performed under applicable regulatory guidelines. The studies included the examination of reproductive and some developmental endpoints and a large range of exposures, including low doses. These

studies include a two-generation reproductive toxicity test in mice and a three-generation reproductive toxicity test in rats.

These studies were considered pivotal in our review of the existing data for a number of reasons. These include: 1) they were conducted in a manner that FDA would recommend to a stakeholder seeking an approval for a new use (i.e., they follow recommended guidelines) including extended parameters allowing for the examination of issues that were controversial to BPA at the time; 2) they were submitted to the Agency with supporting information (raw data) allowing for our independent evaluation of the findings; and 3) they both included a large range of exposures, including a range of high and low doses which allowed for the examination of dose response curves. With regard to FDA's evaluation of BPA, these studies are often given more weight than publications in the public literature that examine the same endpoints because the publications often lack details and supporting data that would be necessary for an independent evaluation of the underlying data by Agency scientists. In addition, many of the published studies on BPA have numerous protocol limitations, including the animal model utilized, the method of BPA measurement, the statistical analysis of the data, the lack of multiple/correctly spaced doses in the experimental protocol, and the route of administration.

By comparing the "no observed effect" level (5 milligrams per kilogram of body weight per day) derived from the reproductive and developmental endpoints examined in these pivotal studies to the estimated daily intake of BPA, FDA determined that an adequate margin of exposure exists to reach a conclusion of "reasonable certainty of no harm under the intended

conditions of use," the standard set forth in 21 CFR §170.3(i). That margin of exposure is approximately 7,000 fold for infants -- that is, the levels of exposure to BPA at which any effects would be observed in infants is about 7,000 times higher than our estimates of actual exposure.

In addition, FDA has completed a summary of the pharmacokinetic data on BPA in multiple species. FDA has determined that understanding the species differences and the differences in how metabolic systems handle BPA administered via various routes of exposure, such as oral versus subcutaneous, are also pivotal to examining the safety of BPA.

FDA's findings thus far are underscored by the conclusions of two risk assessments for BPA from 2006, conducted by the European Food Safety Authority's Scientific Panel of Food Additives, Flavourings, Processing Aids and Materials in Contact with Food, and the Japanese National Institute of Advanced Industrial Science and Technology. Each of these documents considered the possibility of a low-dose effect and concluded that no health risk exists for BPA at the current exposure level. Neither of these risk assessments disagrees with FDA's current position of the safe use of BPA at the current exposure level.

BPA TASK FORCE REVIEW

FDA has carefully studied the review and conclusions of the expert panel convened by CERHR, released on November 26, 2007. The CERHR expert panel found that, based on current BPA exposure levels, "some concern" exists for pregnant women and fetuses and

infants and children for exposure to BPA causing neural and behavioral effects. The expert panel also concluded that there was "minimal concern" for BPA exposure in these populations for effects in the prostate gland, mammary gland, and an earlier age for puberty in females.

The NTP Draft Brief released on April 14, 2008, reiterated the conclusions of the CERHR panel with regard to neural and behavioral effects. However, the NTP Draft Brief departed from the expert panel in concluding that "some concern" exists for effects in the prostate gland, mammary gland, and an earlier age for puberty in females for BPA exposure to fetuses, infants and children. These analyses emphasized relatively new data and emerging or difficult-to-interpret endpoints in toxicology and considered the fact that the studies currently available provide limited evidence and contain numerous uncertainties. It is noteworthy that the increase in concern from "minimal" to "some" from the conclusion from CERHR's expert panel to NTP's Draft Brief reflects numerous studies that have appeared in the literature only in the past several months. Although the NTP Draft Brief discusses "some concern" for developmental exposure and mammary and prostate gland cancer, it also highlights the uncertainties regarding these data and states that the evidence is not sufficient to conclude that BPA is a rodent carcinogen for these endpoints or that BPA presents a cancer hazard to humans.

Neural and behavior development effects were also the focus of a recent draft risk assessment released by Health Canada and Environment Canada on April 18, 2008. Both the NTP Draft Brief and the Canadian draft risk assessment are reviews of existing and recently developed data. Both discuss animal studies on neural, behavioral, and developmental effects and both

assessments point out that these studies provide only limited evidence for concern for human exposure to BPA. Finally, both suggest that more research is needed to better understand their implications for human health.

FDA has not yet completed its review of concerns raised by the CERHR expert panel last fall or the NTP Draft Brief released last month. Therefore, those concerns are under active consideration by FDA centers and the BPA Task Force, and we will take appropriate action, if warranted, at the completion of our review.

PHTHALATES

Because all of FDA's product centers are represented on the BPA Task Force, Commissioner von Eschenbach has also tasked it with establishing a comprehensive inventory of regulated products that contain phthalates. Phthalates are primarily used as plasticizers in polyvinyl chloride (PVC) and polyvinylidene chloride (PVDC) polymers to increase their flexibility. Di-(2-ethylhexyl) phthalate (DEHP) is perhaps the most thoroughly studied among the phthalates. DEHP has long been used to produce highly flexible versions of PVC and PVDC polymers for a variety of applications, such as in flexible packaging film.

FDA-authorized uses of phthalates include uses in flexible food packaging. Over the past decade, however, such food contact uses have been greatly reduced or eliminated through the replacement of PVC and PVDC polymers with other polymers that do not require plasticizers and by the use of alternative plasticizers in PVC and PVDC. FDA's Center for Food Safety

and Applied Nutrition (CFSAN) has tracked the reductions in use of phthalates in food contact materials as well as the development of new toxicological data.

CFSAN has recently established a Phthalate Task Group (PTG) to review all available use and toxicology information associated with phthalate exposure from food contact use and to better characterize any potential risk from these uses. The primary focus of the PTG will be to determine the most realistic exposure estimation and risk associated with phthalate use in food packaging. The PTG will review and address past studies on phthalates and any new information available. If our review indicates that existing data no longer supports the continued safe use of these materials in food contact material, FDA will take appropriate regulatory action to remove these materials from the marketplace.

There are also significant uses of phthalates in certain medical products, such as intravenous solution bags and medical tubing. FDA's Center for Devices and Radiological Health (CDRH) has looked into the use of polyvinyl chloride using DEHP as a plasticizer in medical devices. DEHP is a chemical ingredient that affords PVC many of the physical properties that make it optimally suited for use in many of today's medical devices.

While toxic and carcinogenic effects of DEHP have been demonstrated in laboratory animals, there are no studies in humans that are adequate to serve as the basis for regulatory decision-making. Further, health care providers should not avoid performing certain medical procedures simply because of the possibility of health risks associated with DEHP exposure.

In these cases, the risk of not doing a needed procedure is far greater than the risk associated with exposure to DEHP.

Phthalates are also widely used in cosmetics, serving as solvents for fragrances, antifoaming and suspension agents, skin emollients, and plasticizers in nail products. CFSAN's Office of Cosmetics and Colors has conducted laboratory surveys of phthalate levels in marketed cosmetics. The last survey indicated that diethylphthalate (DEP) was the most frequently used phthalate in cosmetics and that nail enamels contained the highest levels of phthalates, primarily dibutylphthalate (DBP). Based on the results of that survey and the toxicity data currently available, FDA does not believe that phthalates in cosmetics pose a health risk. Since the survey was conducted, we have observed that some cosmetic products are being reformulated to remove phthalates. CFSAN is planning a more extensive survey of a larger number of cosmetic products to better determine to what extent cosmetic products contribute to total human exposure to phthalates. We will continue to monitor and evaluate all available data to ensure that phthalate levels in cosmetic products are not a health concern.

FDA, primarily through its' National Center for Toxicological Research (NCTR), is conducting further research to address uncertainties in our understanding of the potential health risk posed by exposure to phthalates. Much of the concern on medical exposures to phthalates is focused on potential reproductive tract effects in male infants in neonatal intensive care units, a population exposed to high levels of DEHP at a sensitive period of development. The NCTR studies are evaluating the metabolism and toxicity of DEHP

following intravenous exposure in infant male nonhuman primates, a model that more closely resembles the human exposure of highest concern.

CONCLUSION

Although the Agency's review of the newly available reports is continuing, a large body of available evidence indicates that currently-marketed food contact materials containing BPA are safe, and that exposure to BPA from food contact materials, including exposures for infants and children, are below the levels that may cause health effects. We are actively reviewing the data on BPA and will continue to consider the relevance of new data and studies as they appear.

In the case of both BPA and phthalates, FDA's work in assessing the safety of products that contain these chemicals is never truly final, and if our continuing review of all available data leads us to a determination that the current levels of exposure are not safe, we will take appropriate action to protect the public health. Thank you for the opportunity to testify today, and I would be happy to answer any questions.